

Application No.: 09/701,586

Inventor: Kock et al.

Reply to Office Action of 11 January 2006

Docket No.: 49100

Amendments to the Claims:

1. (currently amended) An isolated and purified poly(ADP-ribose) polymerase (PARP) homolog comprising human PARP2 (SEQ ID NO: 2) or a functional equivalent thereof which is at least 85% homologous thereto, exhibits poly(ADP-ribose)-synthesizing activity, and has an amino acid sequence which
 - a) has a functional NAD⁺ binding domain comprising the sequence motif $PX_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:11) in which n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid;
and
 - b) lacks a zinc finger sequence motif of the **general** formula $CX_2CX_mHX_2C$ (SEQ ID NO:30) in which m is an integral value of 28 or 30, and the X radicals are, independently of one another, any amino acid.
2. (currently amended) The PARP homolog as claimed in claim 1, wherein the functional NAD⁺ binding domain comprises **one of** the following **general** sequence motifs:
 $(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFA$ (SEQ ID NO:12) or
 $LLWHG(S/T)X_2IL(S/T)XGLR(I/V)XPX_n(S/T)GX_3GKGIYFA$,
 $X_2GKGIYFA$,
 $SKSAXY$ (SEQ ID NO:13)
in which n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid.
3. (currently amended) The PARP homolog as claimed in claim 1, **further** comprising at **least another one of the following** part-sequence motifs:
 $LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$ (SEQ ID NO: 15);
 $AX_3FXKX_4KTXNXWX_5FX_3PXK$ (SEQ ID NO:16),

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QXL₁(I/L)X₂IX₃MX₄PLGKLX₅QIX₆L (SEQ ID NO:17),

FYTXIPHGX₃PP (SEQ ID NO:18); and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19),

in which the X radicals are, independently of one another, any amino acid.

4-32. (canceled)

33. (new) The PARP homolog as claimed in claim I, wherein the functional NAD⁺ binding domain comprises the following sequence motif:

LLWHG(S/T)X₇IL(S/T)XGLR(I/V)XPX_n(S/T)GX₃GKGIYFAX₃SKSAXY (SEQ ID NO:13)

in which n is an integral value from 1 to 5, and

the X radicals are, independently of one another, any amino acid.

34. (new) The PARP homolog as claimed in claim I further comprising part-sequence motif

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16)

in which the X radicals are, independently of one another, any amino acid.

35. (new) The PARP homolog as claimed in claim I further comprising part-sequence motif

XL(I/L)X₂IX₃MX₄PLGKLX₅QIX₆L (SEQ ID NO:17)

in which the X radicals are, independently of one another, any amino acid.

36. (new) The PARP homolog as claimed in claim I further comprising part-sequence motif

FYTXIPHGX₃PP (SEQ ID NO:18)

in which the X radicals are, independently of one another, any amino acid.

37. (new) The PARP homolog as claimed in claim I further comprising part-sequence motif

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

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in which the X radicals are, independently of one another, any amino acid.

38. (new) An isolated poly(ADP-ribose) polymerase (PARP) homolog comprising human PARP2 (SEQ ID NO: 2) or a functional equivalent thereof which is at least 85% homologous thereto, exhibits poly(ADP-ribose)-synthesizing activity, and has an amino acid sequence which

a) has a functional NAD⁺ binding domain comprising the sequence motif

PX_n(S/T)GX₃GKGIYFA (SEQ ID NO:11)

in which n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid;

and

b) lacks a zinc finger sequence motif of the formula

CX₂CX_mHX₂C (SEQ ID NO:30)

in which m is an integral value of 28 or 30, and the X radicals are, independently of one another, any amino acid

further comprising a leucine zipper-like sequence motif:

(L/V)X₆LX₆LX₆L

wherein X radicals are, independently of one another, any amino acid.

39. (new) The PARP homolog as claimed in claim 38 further comprising at least one of the following part-sequence motifs:

-----LX₉NX₂YX₂QLLX(D/E)X_{10'11}WGRVG (SEQ ID NO: 15),-----

AX₃FXKX₄KTXNXWX₃FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid.

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40. (new) The PARP homolog as claimed in claim 38 further comprising part-sequence motifs:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15)

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHXFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid.

41. (new) The PARP homolog as claimed in claim 38 further comprising part-sequence motifs:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15)

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHXFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid, wherein

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG

is closest to the N terminus.

42. (new) The PARP homolog as claimed in claim 1 further comprising part-sequence motifs:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15)

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHXFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid.

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43. (new) The PARP homolog as claimed in claim 1 further comprising part-sequence motifs:

$LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$ (SEQ ID NO: 15)

$AX_3FXKX_4KTXNWX_5FX_3PXK$ (SEQ ID NO:16),

$QXL(I/L)X_2IX_9MX_{10}PLGKLX_3QIX_6L$ (SEQ ID NO:17),

$FYTXIPHFGX_3PP$ (SEQ ID NO:18), and

$KX_3LX_2LXDIEXAX_2L$ (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid, wherein

$LX_9NX_2YX_2QLLX(D/E)X_{10/11}WGRVG$

is closest to the N terminus.

44. (new) The PARP homolog as claimed in claim 1 further comprising at least one of the following:

$GX_3LXVALG$,

$GX_2SX_4GX_3PX_aLXGX_2V$, and

$E(Y/F)X_2YXYX_3QXYLL$

in which a is 7 to 9 and

X is any amino acid.

45. (new) The PARP homolog as claimed in claim 1 further comprising

~~$GX_3LXEVALG$~~ ,

$GX_2SX_4GX_3PX_aLXGX_2V$, and

$E(Y/F)X_2YX_3QX_4YLL$

in which a is 7 to 9 and

X is any amino acid.

46. (new) The PARP homolog as claimed in claim 1 further comprising

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$\text{GX}_3\text{LXEVALG}$,
 $\text{GX}_2\text{SX}_4\text{GX}_3\text{PX}_a\text{LXGX}_2\text{V}$, and
 $\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

in which a is 7 to 9 and

X is any amino acid, wherein

$\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

is closest to the C terminus.

47. (new) An isolated poly(ADP-ribose) polymerase (PARP) homolog comprising human PARP2 (SEQ ID NO: 2) or a functional equivalent thereof which is at least 85% homologous thereto, exhibits poly(ADP-ribose)-synthesizing activity, and has an amino acid sequence which

- has a functional NAD^+ binding domain comprising the sequence motif $\text{PX}_n(\text{S/T})\text{GX}_3\text{GKGIYFA}$ (SEQ ID NO:11) in which n is an integral value from 1 to 5, and the X radicals are, independently of one another, any amino acid;

and

- lacks a zinc finger sequence.

48. (new) The PARP homolog as claimed in claim 47 wherein said PARP lacks a zinc finger sequence motif of the formula

$\text{CX}_2\text{CX}_m\text{HX}_2\text{C}$ (SEQ ID NO:30)

in which m is an integral value of 28 or 30, and the X radicals are, independently of one another, any amino acid.

49. (new) The PARP homolog as claimed in claim 47 wherein the functional NAD^+ binding domain comprises the following sequence motif:

$(\text{S/T})\text{XGLR(I/V)}\text{XPX}_0(\text{S/T})\text{GX}_3\text{GKGIYFA}$ (SEQ ID NO:12)

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in which n is an integral value from 1 to 5, and
the X radicals are, independently of one another, any amino acid.

50. (new) The PARP homolog as claimed in claim 47 wherein the functional NAD⁺ binding domain comprises the following sequence motif:

LLWHG(S/T)X₇IL(S/T)XGLR(I/V)XPX_n(S/T)GX₃GKGIYFAX₃SKSAXY (SEQ ID NO:13)

in which n is an integral value from 1 to 5, and
the X radicals are, independently of one another, any amino acid.

51. (new) The PARP homolog as claimed in claim 47 further comprising a leucine zipper-like sequence:

(L/V)X₆LX₆LX₆L

wherein X radicals are, independently of one another, any amino acid.

52. (new) The PARP homolog as claimed in claim 51 further comprising at least one of the following part-sequence motifs:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15),

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHXFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid.

53. (new) The PARP homolog as claimed in claim 51 further comprising:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15),

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

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FYTXIPHFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid.

54. (new) The PARP homolog as claimed in claim 51 further comprising:

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG (SEQ ID NO: 15),

AX₃FXKX₄KTXNXWX₅FX₃PXK (SEQ ID NO:16),

QXL(I/L)X₂IX₉MX₁₀PLGKLX₃QIX₆L (SEQ ID NO:17),

FYTXIPHFGX₃PP (SEQ ID NO:18), and

KX₃LX₂LXDIEXAX₂L (SEQ ID NO:19)

in which the X radicals are, independently of one another, any amino acid, wherein

LX₉NX₂YX₂QLLX(D/E)X_{10/11}WGRVG

is closest to the N terminus.

55. (new) The PARP homolog as claimed in claim 47 further comprising at least one of the following:

GX₃LXVALG,

GX₂SX₄GX₃PX_aLXGX₂V, and

E(Y/F)X₂YX₃QX₄YLL

in which a is 7 to 9 and

X is any amino acid.

56. (new) The PARP homolog as claimed in claim 47 further comprising

GX₃LXEVALG,

GX₂SX₄GX₃PX_aLXGX₂V, and

E(Y/F)X₂YX₃QX₄YLL

in which a is 7 to 9 and

X is any amino acid.

57. (new) The PARP homolog as claimed in claim 47 further comprising

$\text{GX}_3\text{LXEVALG}$,
 $\text{GX}_2\text{SX}_4\text{GX}_3\text{PX}_a\text{LXGX}_2\text{V}$, and
 $\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

in which a is 7 to 9 and

X is any amino acid, wherein

$\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

is closest to the C terminus.

58. (new) The PARP homolog as claimed in claim 51 further comprising at least one of the following:

GX_3LXVALG ,
 $\text{GX}_2\text{SX}_4\text{GX}_3\text{PX}_a\text{LXGX}_2\text{V}$, and
 $\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

in which a is 7 to 9 and

X is any amino acid.

59. (new) The PARP homolog as claimed in claim 51 further comprising

$\text{GX}_3\text{LXEVALG}$,
 $\text{GX}_2\text{SX}_4\text{GX}_3\text{PX}_a\text{LXGX}_2\text{V}$, and
 $\text{E(Y/F)X}_2\text{YX}_3\text{QX}_4\text{YLL}$

in which a is 7 to 9 and

X is any amino acid.

60. (new) The PARP homolog as claimed in claim 51 further comprising

$\text{GX}_3\text{LXEVALG}$,
 $\text{GX}_2\text{SX}_4\text{GX}_3\text{PX}_a\text{LXGX}_2\text{V}$, and

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E(Y/F)X₂YX₃QX₄YLL

in which a is 7 to 9 and

X is any amino acid, wherein

E(Y/F)X₂YX₃QX₄YLL

is closest to the C terminus.